IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: **Brauckman, Richard A.**

Serial No.: **09/858,366** Group Art Unit: **3732**

Filed: **May 16, 2001** Examiner: **Ramana, Anuradha**

For: **CATHETER ATTACHMENT AND CATHETER FOR BRACHYTHERAPY**

DECLARATION OF DR. JOHN LOBDELL PURSUANT TO 37 C.F.R. §1.132

Assistant Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

1. I, Dr. John Lobdell, hereby declare as follows:

2. I am an employee of the Theragenics Corporation and have 36 years experience in the nuclear industry. My detailed *curriculum vitae* is attached hereto as Exhibit A.

3. I have reviewed the specification, drawings and currently pending claims of U.S. patent application no. 09/858,366. I have also reviewed the Office Action mailed on May 20, 2004 (hereinafter "the Office Action").

4. I am informed that claims 1-6 of the present application stand rejected under 35 U.S.C. §112, 1st paragraph, as failing to comply with the enablement requirement on the basis that, "It is the Examiner's position that 'sufficient bond strength' cannot be determined without undue experimentation."

5. I am informed that the standard for determining whether the specification meets the enablement requirement was set forth in *Mineral Separation v. Hyde*, 242 U.S. 261, 270 (1916), which posed the question, "is the experimentation needed to practice the invention undue or unreasonable?"

6. I am also informed that the factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to:

(A) The breadth of the claims;

(B) The nature of the invention;

(C) The state of the prior art;

(D) The level of one of ordinary skill;

(E) The level of predictability in the art;

(F) The amount of direction provided by the inventor;

(G) The existence of working examples; and

(H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

In re Wands, 858 F.2d 731,737,8 USPQ2d 1400, 1404 (Fed.Cir.1988) and MPEP §2164.01(a).

Claim 1

7. With regard to the breadth of the claims at issue, claim 1 of the present application is relatively narrow in scope since it requires a radioactive source bonded to a surface of the distal section of an elongate, flexible catheter body with sufficient bond strength that under normal conditions of use of the catheter, this radioactive source will not detach from the catheter body when in use.

8. With regard to the nature of the invention, the invention relates to a catheter useful for radiation treatment, wherein the catheter has a radioactive source bonded to a surface of the distal section of the catheter such that when the catheter is used the bonded radioactive source does not detach from the catheter. Since catheters provided with radioactive material have been known for quite some time, as evidenced by U.S. Patent nos. 5,199,939 and 5,282,781, the nature of the invention is to provide an improvement

to existing catheters with radioactive material. As such, the invention lies in the improved positioning and manner whereby the radioactive material is associated with the catheter. Accordingly, since the nature of the invention is not unduly complex and relates to the provision of an improvement of conventional devices, it is my opinion that the skilled person will have a high degree of knowledge regarding the subject matter of the invention.

9. The state of the prior art is evidenced by, for example, two of the documents of record in the present application, namely, "U.S. Patent No. 5,199,939 to Dake et al. (hereinafter "the Dake et al. patent"); and "U.S. Patent No. 5,302,168 to Hess (hereinafter "the Hess patent"). The state of the prior art is such that devices similar to the device of the present invention are known from the prior art.

10. The level of ordinary skill in the art is high. Specifically, the user of catheters is, at minimal, highly trained medical personnel such as a medical doctor (MD), a doctor of veterinary medicine (DVM), or medical personnel under the direct supervision of such persons, or possibly a Ph.D. researcher. Often, the designers of catheters are the medical personnel themselves as they are most intimately acquainted with the advantages and disadvantages each type catheter has. Additionally, biomedical engineers who have received specialized training in the art may design medical devices.

11. A very significant amount of direction is provided in the present application for implementation of the device of claim 1. For example, the specification explains that the radioactive source may be chemically or thermally bonded to the catheter. See page 5 lines 16-17. The application also explains that suitable catheter materials are well known in the art. See page 6 lines 1-2. The application explains that suitable methods for bonding the radioactive source to the catheter wall include at least electroless plating, chemical vapor deposition, electroplating, ion implantation, sputtering, physical vapor deposition, and the application of a coating of a polymer matrix having material dispersed therein. See page 7, lines 20-24.

12. In addition, beginning on page 14, line 32, the specification describes the use of a diluent for purposes of promoting strong adhesion of the radioactive source material to the substrate, thereby forming a physiological inert layer which will not allow the radioactive source to be mobilized into the circulation of the patient being treated. See page 15, lines 20-24, and page 16, lines 1-4. A description of the suitable substrates to which the radioactive source is bonded to, or incorporated into, begins on page 16, line 10 and continues though page 17, line 18. The specification explains bonding the radioactive material to the substrate at page 17, line 19 to page 20, line 13.

13. The level of predictability in the art of radioactive catheter manufacturing is high. From the teachings of the present specification, using the well-known standard testing methods discussed below, it is my opinion that the skilled person can make and use catheters in accordance with the subject matter of the claims of the above-identified application.

14. The International Organization for Standardization (ISO), a worldwide federation of national standards bodies, publishes standards regulating sealed radioactive sources. The American National Standards Institute (ANSI) is the primary source and official sales agent in the United States for ISO. ISO has published an International Standard for testing sealed radioactive sources, ISO 2919 (copy attached as Exhibit B hereto). ISO 2919 (2nd Ed 1999-01-15) sets forth the general requirements and classification for sealed radioactive sources. ISO 2919 sets forth detailed performance requirements in Section 6 for a variety of radioactive sources, including those used for medical brachytherapy. In ISO 2919, Table 4 provides for sealed source classification (performance) requirements for typical usage (see page 7). These sources are tested using the criteria for brachytherapy sources.

15. Moreover, in Section 7 of ISO 2919, detailed tests for determining whether medical brachytherapy sources meet the performance requirements of Section 6 of ISO 2919 are set forth. These tests include the temperature, pressure, impact, vibration and puncture tests. Each of these tests has, as one purpose, to determine whether under simulated

conditions of use, the radioactive source is bonded to the substrate in a manner whereby the radioactive source will not detach from the device when in use. Thus, ISO 2919 demonstrates that there are well-known, standardized tests for brachytherapy sources for determining "sufficient bond strength" under simulation conditions of use including temperature, pressure, impact, vibration and puncture resistance.

16. ISO 2919 also refers to the requirement that radioactive sources must be tested for leakage and refers to ISO 9978 for this purpose (See Section 3.4 of ISO 2919). ISO 9978 (copy attached as Exhibit C hereto) provides leakage test methods for radioactive sources. The tests set forth in ISO 9978 include immersion tests, gaseous emanation tests, wipe tests, helium mass spectrometer leakage tests, bubble leakage tests, and water pressurization tests, each of which tests is designed to simulate conditions that may be encountered in use of radioactive brachytherapy devices, such as contact with bodily fluids. Thus, ISO 9978 demonstrates that there are well-known standardized tests for determining if a radioactive source will detach from a substrate by leakage under simulated conditions of use. Brachytherapy sources are tested using the criteria presented in this standard.

17. In my opinion, the skilled person is capable of determining "sufficient bond strength" using one or more of the tests set forth in the well-known international standards ISO 2929 and ISO 9978, discussed above.

18. The U.S. Food and Drug Administration (hereinafter "the FDA") regulates medical devices including radioactive catheters (under the direction of the Center for Devices and Radiological Health). For example the Center for Devices and Radiological Health issued a document entitled, "Guidance for Submission of Premarket Notifications for Photon-Emitting Brachytherapy Sources," on August 2, 2000 (copy attached as Exhibit D hereto) (hereinafter "FDA Guidance"). In the FDA Guidance, Section III.2.B, the applicable guidance and standards for photon-emitting brachytherapy sources are listed. Among the listed standards are the ANSI N43.6-1997 Classification of Sealed Radioactive Sources and the ISO 2919 Sealed Radioactive Sources – General

Requirements and Classification. This demonstrates that the FDA recognizes ISO 2919 as providing suitable test methods for evaluation of brachytherapy devices.

19. In my opinion, essentially no experimentation is required to implement the present invention based on the disclosure of the application as filed, taken in combination with the common general knowledge of a skilled person. As discussed above, the skilled person already knows how to test the bond strength for radioactive sources under typical usage conditions as regulated by the FDA under the guidance of the Center for Devices and Radiological Health (CDRH) using the tests set forth in ISO 2199 and ISO 9978.

Dependent Claims

20. Dependent claims 2-6 further specify the type of catheter body, where the radioactive source is bonded to in relation to the surface of the catheter, a retractable sheath for shielding the radioactive material and the nature of the radioactive material itself. In my opinion, the skilled person can implement these dependent claims with essentially no experimentation by using general knowledge from the art for the same reasons as specified above.

21. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true, and further that the statements were made with the knowledge that willful false statements and the like made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Respectfully submitted,

By: _____
Dr. John Lobdell

Dated: 9/2/04

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Education:

B.S. in Physics with a minor in Mathematics, Spring Hill College, Mobile, Alabama, 1964.

M.S.P.H. in Radiological Hygiene, University of North Carolina at Chapel Hill, 1968.

Ph.D. in Health Physics, Georgia Institute of Technology, 1995. Research Topic: "Dose Rate and Spectral Photon Measurements Around a Large BWR Using a Tissue Equivalent Plastic Scintillator." Advisor: Dr. N. E. Hertel.

Five-week class in Boiling Water Reactor Technology at Browns Ferry Nuclear Plant, 1969.

"Occupational & Environmental Radiation Protection", Harvard School of Public Health, August 19-23, 1985.

"Health Physics in Radiation Accidents", Oak Ridge Associated Universities, September 8-12, 1986.

"Workshop on Measurement Quality Assurance for Ionizing Radiation", National Institute of Standards and Technology (NIST), March 16-18, 1993

"Media Center Appearances", C. S. Armstrong Associates, Inc., September 8, 1994

"Radioactive Waste Packaging, Transportation, and Disposal Workshop", Chem-Nuclear Systems, July 21-24, 1997, and May 22-26, 2000.

Professional Certification:

Certified in Health Physics by the American Board of Health Physics, 1972. Recertified in 1981, 1985, 1989, 1993, 1997, and 2001.

Lead Auditor as defined by ANSI N45.2.23-1978, "Qualification of Quality Assurance Program Audit Personnel for Nuclear Power Plants".

HAZMAT trained and certified to ship radioactive material, July 1997 through May 2003.

Health Physics Work Experience:

July 1964 to August 1966:

Employed by the Alabama and Virginia Departments of Health to operate the counting rooms to determine the radioactive content of environmental samples.

June 1968 to September 1996, employed by the Tennessee Valley Authority, Muscle Shoals, AL

From June 1968 to December 1979, I supervised the operation of the following programs: environmental radiological monitoring around TVA's nuclear power plants, health physics training, applied health physics services, film badge and TLD personnel monitoring services, whole body counting, and calibration of portable radiation survey instrumentation.

From December 1979 to May 1980, I coordinated within TVA the modification of the radiological emergency plan for all of TVA's operating nuclear power plants in compliance with NUREG-0654 "Criteria for Preparation and Evaluation of Radiological Emergency Response Plans and Preparedness in Support of Nuclear Power Plants".

From June 1980 to May 1982, I supervised a Quality Assurance/ALARA Staff. The Staff provided quality assurance services to a large health physics organization.

From June 1982 to April 1985, I was the Staff Health Physicist in the office of the Chief, Health Physics Services. I provided health physics expertise to the Chief and all sections within the organization. During a ten-month period, I was assigned to the Browns Ferry Nuclear Plant as the health physicist on a recirculation pipe replacement project on unit 1.

From May 1985 to October 1986, I supervised a Dosimetry Section that coordinated and provided direction for the internal and external dosimetry programs in TVA.

From November 1986 to September 1996, I supervised a section that repaired, maintained, modified, and calibrated portable radiation survey instrumentation.

January 1997 to August 2003: employed by Novoste Corporation, Atlanta, GA.

Novoste is a company that has developed a vascular brachytherapy system for the reduction of restenosis in coronary arteries. I was the Principal Radiation Physicist. When I initiated

employment, the company had no radioactive materials license. The company acquired a research and development license and a manufacturing broad scope license through the State of Georgia. I was the Radiation Safety Officer for these licenses.

During this period, I accomplished the following:

- planned and developed the laboratory that receives, tests, calibrates, and ships ^{90}Sr sources in transfer devices throughout the world,
- performed all the test method validations, installation qualifications, and process hazard analyses for the laboratory,
- developed the techniques for the calibration of the source trains traceable to the National Institute of Standards and Technology,
- set up and developed all the procedures for the operation of the laboratory,
- calculated doses rates from the ^{90}Sr sources using Monte Carlo computer codes,
- designed shielding for the transfer devices using the Monte Carlo codes,
- provided input to FDA on radiation issues,
- developed and gave training programs for company personnel.

During the period, I traveled extensively throughout the US and Western Europe to interface with users, partners, and regulatory agencies.

September 2003 to Present: employed by Theragenics Corporation, Buford, GA

During this period, I am the Director of Health Physics and the Radiation Safety Officer. Theragenics manufactures radioactive seeds containing ^{125}I and ^{103}Pd for the treatment of prostate cancer.

June 1991 to 1995:

I served as a Technical Expert for the National Voluntary Laboratory Accreditation Program (NVLAP) for the Secondary Calibration for Ionizing Radiation Laboratory Accreditation Program.

Teaching Experience: September 1989 to August 1991:

I taught four subjects at Shoals Community College: physics with calculus, two classes in physics without calculus, and health physics for radiographers. I taught a total of 14 quarters.

Significant Papers and Publications:

"Suitability of Glass-Encapsulated CaF_2:Mn Thermoluminescent Dosimeters for Environmental

Radiation Surveillance", presented at the National Health Physics Society Meeting in Miami, June 1973.

"A TLD System for Personnel Monitoring", presented at the meeting of the Deep South and Alabama Chapters of the Health Physics Society, Gulf Shores, Alabama, August 1977.

"Training for a Viable Nuclear Power Plant Radiological Emergency Plan", presented at the Thirteenth Midyear Topical Symposium of the Health Physics Society, Honolulu, December 1979.

"Health Physics Planning for Recirculation Pipe Replacement at a BWR", presented at the annual meeting of the American Nuclear Society, New Orleans, June 1984.

"Calibration of DMC-90s in TVA", presented at the Merlin Gerin User's Group Meeting, Atlanta, April 1992.

"A Tissue Equivalent Detector Photon Response Matrix", presented at the winter meeting of the American Nuclear Society, San Francisco, October 1995.

"Dose Rate And Spectral Photon Measurements Around A Large BWR" presented at the Annual Health Physics Society Meeting, Seattle, July 1996.

"Scanning Personnel For Internal Deposition Of Radioactive Material With Personnel Contamination Whole Body Friskers And Portal Monitors" presented at the Annual Health Physics Society Meeting, Seattle, July 1996.

"Photon Spectra and Dose Measurements Using a Tissue-Equivalent Plastic Scintillator", Radiation Protection Dosimetry, Vol.72, No.2, pp.95-103 (1997).

"Gamma Ray Dose Rate Measurements at a Boiling Water Reactor", Radiation Protection Dosimetry, Vol.74, No.3, pp.163-171 (1997).

"Radiochromic Film Dosimetry of a High Dose Rate Beta Source for Intravascular Brachytherapy", Medical Physics, 26 (11), November 1999.

"Attenuation of Dose From a ^{90}Sr/Y Line Source by a Stainless-Steel Stent", Second Annual Radiotherapy Conference to Reduce Restenosis, La Jolla, CA, January 16-17, 1998.

"Dosimetry and Radiation Aspects of the Use of ^{90}Sr-^{90}Y for Intravascular Brachytherapy", Council on Ionizing Radiation Measurement and Standards, Gaithersburg, MD, October 30 – November 1, 2000.

"Quality Control for Novoste ^{90}Sr-^{90}Y Intravascular Brachytherapy Sources", Council on Ionizing Radiation Measurements and Standards, Gaithersburg, MD, October 29-31, 2001.

"Dose Distribution Superimposed on Cine Images Acquired During IVBT", Cardiovascular Radiation Therapy , February 6-8, 2002.

"Display of Dose Distribution of Cine/Fluoro Images Acquired During IVBT", AAPM Annual Meeting, Montreal, Canada, July 14-18, 2002.

"Dosimetric Characterization of a New $^{90}Sr/^{90}Y$ Source with Balloon for Intravascular Brachytherapy", AAPM Annual Meeting, Montreal, Canada, July 14-18, 2002.

"Monte Carlo Dose Characterization of a New $^{90}Sr/^{90}Y$ Source with Balloon for Intravascular Brachytherapy", Medical Physics, 30 (1), January 2003.

"Dosimetry for a Brachytherapy Implant of a Hemodialysis Graft", AAPM Annual Meeting, Pittsburgh, PA, July 25-29, 2004.